

# Debate

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### View 2: Assisted conception in couples with HIV infection

G P Taylor

Sharma *et al* discuss the fertility needs of HIV affected couples and present a strong case that they should not be denied access to medical interventions to help them conceive while minimising the risks of transmission. Artificial insemination of partner's semen (AIH) is a simple, cheap, and effective method of avoiding HIV transmission from an HIV infected female to her HIV uninfected partner. Prevention of male to female transmission of HIV while trying to conceive is more complicated. To date, sperm washing has proved to be a safer alternative to timed unprotected intercourse with more than 3000 cycles (of insemination of washed sperm) undertaken without transmission. This represents at least a 3–6-fold reduction in risk compared to the reported transmission rates of 1:500 to 1:1000 per episode of unprotected intercourse between uninfected females and their infected partners.<sup>1</sup> There is also a case for offering this service to HIV infected concordant couples to prevent transmission of new viral strains, particularly strains with drug resistance mutations although transmission rates are uncertain.

What then are the arguments against offering this service? Does the argument that medical practitioners should "first do no harm" apply? In relation to the couples—clearly not. The intervention, be it advice or sperm washing, reduces their risk and "safer conception" has no less merit than "safer sex."

In relation to the planned conceptus the case might seem less watertight, particularly if the intervention places the baby at risk of HIV infection. The best evidence indicates that with antiretroviral therapy, prelabour caesarean section, and complete avoidance of breast feeding the risk of HIV transmission to the baby is less than 1%.<sup>2</sup> How much less than 1%, remains unknown and transmission has been reported despite triple therapy.<sup>3</sup> Another approach is to consider not the number of drugs in the combination but their efficacy. What is the risk of transmission if HIV cannot be detected in plasma? Certainly transmissions have been reported with undetectable plasma viraemia when the limit of detection has been 500–1000 HIV RNA copies/ml.<sup>4</sup> Unfortunately, robust data on the transmission rates with viral load less than 50 have not been reported although many believe the rates will be significantly less than 1%.

Does pregnancy affect the health of the HIV positive mother? Even before effective antiretroviral combination therapy this appeared not to be the case, although in one study a more rapid decline in CD4+ T lymphocytes was reported post partum. Unpublished data from a London cohort indicate a very low rate of HIV related disease and no deaths following pregnancy among more than

200 women followed for a mean of 2 years. Data such as these also help to address concerns that HIV uninfected children might suffer because of parental ill health or death. Although Sharma *et al* assert that survival of at least 20 years is now possible and indeed long term non-progression is well recognised, for the majority experience with effective antiretroviral therapy is limited to 5–6 years and the problems of drug resistance and toxicity are emerging.

Is the conceptus at any other risk? As outlined above to reduce the risk of mother to child transmission the fetus and the neonate will be exposed to one or more antiretroviral medications. If the mother requires antiretroviral therapy for her own health before conception the embryo will be exposed to at least three drugs with the attendant possibility that organogenesis might be disturbed. In this regard the data emerging from the Antiretroviral Pregnancy Registry are encouraging.<sup>5</sup> No pattern of increased risk of congenital malformation has been observed for any class of antiretroviral drug and sufficient prospective data have been gathered to exclude a greater than twofold increased risk for five individual compounds—namely, zidovudine, lamivudine, neftinavir, stavudine, and nevirapine. However, given that more than 100 permutations of combinations exist risk associated with any particular regimen is difficult to determine.

New concerns relating to exposure at any time during gestation and/or post-delivery are emerging. Do combinations result in an increased risk of preterm delivery?<sup>6</sup> Is the exposure to nucleoside analogues sufficient to cause mitochondrial toxicity in the infant and if so will this have significant long term effect?<sup>7</sup>

Where does this leave the physician? This is perhaps the wrong question. Data from the United Kingdom<sup>8</sup> and elsewhere demonstrate an increasing incidence of pregnancy among women on combination antiretroviral therapy and anecdotal evidence suggests that many are women who have practised contraception for many years and now wish to start or extend their family. Many have or have had children with HIV infection and understand better than anyone the impact of this condition. Their reasons are many, personal, family, social and cultural, but the importance of fertility alongside other aspects of physical, mental, and spiritual wellbeing should not be underrated. They choose to conceive now because they understand that the risks of transmission have been substantially reduced while their prospects of surviving to raise their children have significantly increased.

In the clinic, preconceptual advice is increasingly sought. Following a discussion of the pros and cons, the known and unknown, as outlined

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above, we support women who wish to conceive. This includes advice on "safer conception" as well as investigation and management of infertility. Currently, the major concern is the lack of provision of sperm washing, which is beyond the resources of the majority, by the NHS.

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